

The Synthesis of Cancer-Producing Compounds

A DISSERTATION

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
IN THE UNIVERSITY OF MICHIGAN

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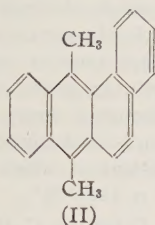
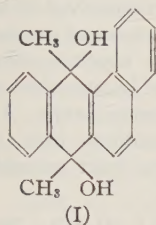


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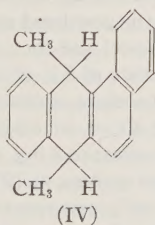
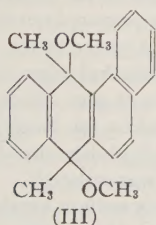
The Synthesis of 9,10-Dimethyl-1,2-benzanthracene, 9,10-Diethyl-1,2-benzanthracene and 5,9,10-Trimethyl-1,2-benzanthracene

BY W. E. BACHMANN AND J. M. CHERMERDA¹

Recently 9,10-dimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene (I) was synthesized from 1,2-benzanthraquinone and methylmagnesium iodide.² This compound offered us the opportunity of obtaining 9,10-dimethyl-1,2-benzanthracene (II), a compound of particular in-

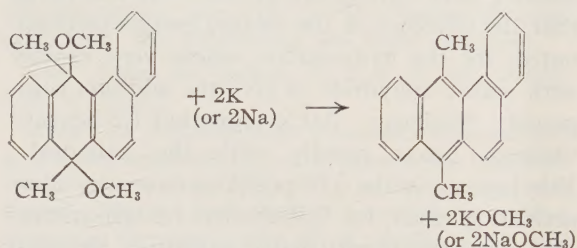


terest because of its close relation to a number of potent carcinogenic hydrocarbons. Treatment of the diol with reducing agents such as hydriodic acid or zinc and acetic acid failed to give the desired hydrocarbon. The hydrocarbon was finally obtained in the following manner. The diol was converted to its dimethyl ether (III) by reaction with methanol in the presence of a small amount of sulfuric acid. Treatment of the dimethyl ether with 45% sodium amalgam replaced the methoxy groups by sodium atoms to yield the intensely colored 9,10-disodio-9,10-dimethyl-9,10-dihydro-1,2-benzanthracene, from which 9,10-dimethyl-9,10-dihydro-1,2-benzanthracene (IV) was obtained by reaction with methanol. The dihydro compound was dehydrogenated by sulfur to the desired 9,10-dimethyl-1,2-benzanthracene. By this method 20-30% yields of the hydrocarbon were obtained from the diol dimethyl ether.

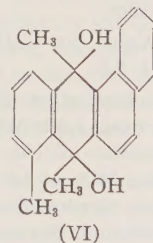
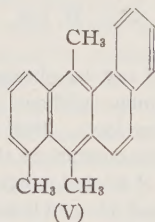


A simpler and much better method of converting the dimethyl ether of the diol to 9,10-dimethyl-1,2-benzanthracene was discovered in the use of

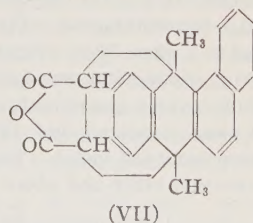
exactly two atomic equivalents of potassium or sodium. The mechanism of the reaction is still under investigation but the over-all reaction may be written as follows



Through this reaction 9,10-dimethyl-1,2-benzanthracene was obtained directly from the dimethyl ether of the diol in yields as high as 96% (or 72% on the basis of the readily available 1,2-benzanthraquinone). The same procedure gave an equally high yield of 9,10-diethyl-1,2-benzanthracene from the dimethyl ether of 9,10-diethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene. At the end of the reaction between the dimethyl ether and potassium, the reaction mixture was perfectly colorless. In a similar manner we have prepared 5,9,10-trimethyl-1,2-benzanthracene (V) from the diol (VI), which was obtained by interaction of 5-methyl-1,2-benzanthraquinone and methylmagnesium iodide.



The reaction between 9,10-dimethyl-1,2-benzanthracene and maleic anhydride to form the addition product (VII) was of interest in view of



(1) From part of the Ph.D. dissertation of J. M. Chermersda.
 (2) Bachmann and Bradbury, *J. Org. Chem.*, **2**, 175 (1937).

some results which we reported recently on the rate of addition of maleic anhydride to polycyclic hydrocarbons.³ We had found that methyl groups in the 9,10-positions of anthracene greatly increased the reactivity of these positions with respect to addition of maleic anhydride, while a 1,2-benzo group decreased the reactivity of the molecule. In 9,10-dimethyl-1,2-benzanthracene both the activating methyl groups and the inhibiting benzo group are present. It was found that the influence of the methyl groups predominated, for the hydrocarbon reacts very rapidly with maleic anhydride to give the addition compound. Similarly, 5,9,10-trimethyl-1,2-benzanthracene reacts rapidly with the anhydride. Ethyl groups in the 9,10-positions have very little activating effect, for 9,10-diethyl-1,2-benzanthracene reacts slowly with maleic anhydride, although more rapidly than does 1,2-benzanthracene.

Experimental

9,10-Dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene (III).—A mixture of 0.25 cc. of concentrated sulfuric acid in 10 cc. of methanol was added to a solution of 5.0 g. of 9,10-dimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene² in 20 cc. of methanol. After a few minutes the dimethyl ether of the diol began to crystallize from the solution. After half an hour, 4.5 g. of the product was filtered off; from the filtrate an additional 0.5 g. was isolated, making a total yield of 91%. The dimethyl ether was freed from traces of sulfuric acid by dissolving it in benzene, shaking the solution with dilute ammonium hydroxide, concentrating the solution to a small volume and adding methanol. The dimethyl ether of the diol crystallizes from benzene-methanol in colorless needles; m. p. 173.5–174.5°. With concentrated sulfuric acid it gives a dark red color.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 83.0; H, 6.8. Found: C, 83.4; H, 6.8.

The dimethyl ether of the diol can be obtained conveniently from 1,2-benzanthraquinone without isolating the intermediate diol in crystalline form. Half an hour after adding 10 g. of 1,2-benzanthraquinone to the Grignard reagent prepared from 10 cc. of methyl iodide and 3.6 g. of magnesium in 60 cc. of ether and 60 cc. of benzene, the mixture was hydrolyzed with ice-cold ammonium hydroxide solution. The ether-benzene solution was concentrated to a small volume and 30 cc. of methanol containing 0.5 cc. of sulfuric acid was added. In this manner 9.2 g. (75%) of the dimethyl ether of the diol was obtained.

9,10-Dimethyl-1,2-benzanthracene.—Five cc. of dry benzene was placed in a warm 30-cc. cylinder fitted with a glass stopper; 0.50 g. of potassium was added, the mixture was heated carefully over a steam-bath until the metal melted, the flask was stoppered and the mixture was shaken in order to powder the metal. Two grams of the aforementioned dimethyl ether and about a dozen sharp

particles of glass (made from a glass rod) were introduced and the flask was then filled with anhydrous ether. After the stopper had been sealed with Meloche and Fredrick grease⁴ and tied down, the mixture was placed on a revolving wheel. After being agitated for sixteen to twenty hours the mixture had a greenish color, which was removed completely by one drop of methanol; no potassium remained. The solution was washed with dilute hydrochloric acid, filtered and evaporated, and the residue was recrystallized from acetone-alcohol. The first crop of nearly colorless hydrocarbon weighed 1.44 g. and melted at 121.5–123°; from the filtrate an additional 0.1 g. of hydrocarbon melting at 119–121° was obtained, making a total yield of 96%. For purification the hydrocarbon and twice its weight of picric acid were dissolved in hot absolute alcohol; the picrate which precipitated on cooling was recrystallized once or twice from absolute ethanol. A benzene solution of the regenerated hydrocarbon was then passed through a tower of aluminum oxide. The 9,10-dimethyl-1,2-benzanthracene crystallizes from acetone-alcohol in leaflets which possess a faint greenish-yellow tinge; m. p. 122–123°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.7; H, 6.3. Found: C, 93.4; H, 6.2.

The hydrocarbon is readily soluble in benzene, moderately soluble in acetone and only slightly soluble in alcohol.

On cooling a solution of 9,10-dimethyl-1,2-benzanthracene and twice its weight of picric acid in hot absolute alcohol the monopicate crystallized in beautiful black needles. After being recrystallized from absolute alcohol, the **monopicate** melted sharply at 112.5–113°.

Anal. Calcd. for $C_{20}H_{16} \cdot C_6H_3O_7N_3$: N, 8.6. Found: N, 8.6.

When a suspension of the monopicate and crystals of picric acid in cold absolute alcohol was allowed to stand for twenty-four hours, the black crystals of the monopicate were replaced by fine reddish-brown needles of the dipicate. The latter can be obtained directly from the solution if four to five moles of picric acid are used for each mole of hydrocarbon. The **dipicate** does not melt sharply; it begins to sinter at about 95° but does not melt until 102–106°.

Anal. Calcd. for $C_{20}H_{16} \cdot 2C_6H_3O_7N_3$: N, 12.3. Found: N, 12.3.

The reaction of the diol dimethyl ether with sodium was carried out in the same manner as for potassium, except that the powdered sodium was prepared outside of the reaction vessel and then transferred to the latter. In one run a mixture of 5 g. of the diol dimethyl ether, 0.75 g. of powdered sodium, a dozen particles of glass, 20 cc. of benzene and 40 cc. of ether was shaken for twenty hours. From the mixture 3.6 g. (90%) of 9,10-dimethyl-1,2-benzanthracene melting at 121.5–123° was isolated.

In the early experiments in which sodium amalgam was employed, 1.0 g. of the diol dimethyl ether and 10 g. of 45% sodium amalgam in 30 cc. of ether and 30 cc. of benzene were shaken in the absence of air for four days. The deep green color which was formed initially gradually gave way to an intense red color. The amalgam was frozen by plac-

(3) Bachmann and Kloetzel, *THIS JOURNAL*, **60**, 481 (1938).

(4) Meloche and Fredrick, *ibid.*, **54**, 3264 (1932).

ing the flask in ice water and the solution was decolorized by the addition of methanol. The oily residue (IV) obtained by evaporation of the ether-benzene solution was heated with 0.2 g. of sulfur at 200° for one-half hour. The 9,10-dimethyl-1,2-benzanthracene which was formed by the dehydrogenation process was sublimed from the mixture and purified by the methods already described. The yield of hydrocarbon (m. p. 122–123°) varied, usually amounting to 20–30% of the calculated amount.

9,10 - Dimethyl-1,2-benzanthracene-9,10-endo- α,β -succinic Anhydride (VII).—A solution of 0.5 g. of 9,10-dimethyl-1,2-benzanthracene and 0.25 g. of maleic anhydride in 5 cc. of benzene was refluxed for one hour. The orange-yellow color originally present gradually disappeared and the solution was nearly colorless after twenty minutes (in another experiment it was found that the reaction was 94% complete in this time). On cooling, 0.6 g. of the addition compound crystallized in colorless needles. The compound is readily soluble in ethyl acetate but little soluble in benzene and it may be recrystallized from a mixture of the two solvents; m. p. 238–240° with decomposition.

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 81.3; H, 5.1. Found: C, 81.1; H, 5.1.

9,10 - Diethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene.—A 94% yield of the dimethyl ether was obtained when a solution of 5 g. of 9,10-diethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene³ in 15 cc. of warm methanol was cooled and treated with a solution of 0.25 cc. of concentrated sulfuric acid in 10 cc. of methanol. The product was purified in the manner described for the methyl analog. The compound can also be obtained conveniently from 1,2-benzanthraquinone without isolation of the intermediate diol by following the procedure outlined for the methyl compound. Any 1,2-benzanthraquinone present in the solution of the crude diol can be extracted by a concentrated solution of sodium hydrosulfite and sodium hydroxide. From benzene-methanol the diol dimethyl ether crystallizes in colorless needles; m. p. 172–173°. With concentrated sulfuric acid it gives an intense red color.

Anal. Calcd. for $C_{24}H_{26}O_2$: C, 83.2; H, 7.6. Found: C, 82.6; H, 7.6.

9,10-Diethyl-1,2-benzanthracene.—A mixture of 2.0 g. of the aforementioned diol dimethyl ether and 0.46 g. of powdered potassium was allowed to react under the conditions described for the methyl analog. After twenty hours, no potassium remained and the solution was perfectly colorless, containing a white suspension of potassium methylate. From the mixture was isolated 1.58 g. (96%) of 9,10-diethyl-1,2-benzanthracene melting at 97–99°. After being purified through the picrate and by passage of its benzene solution through aluminum oxide, the hydrocarbon melted at 98.5–99.5°. 9,10-Diethyl-1,2-benzanthracene crystallizes from acetone-alcohol in thin, perfectly colorless plates. The hydrocarbon was obtained in yields of 90% or more by reaction of the diol dimethyl ether with powdered sodium.

Anal. Calcd. for $C_{22}H_{20}$: C, 92.9; H, 7.1. Found: C, 92.5; H, 6.8.

Since the picrate dissociates readily into the two components in hot alcohol, it was made with excess of picric acid present. The crystals of picric acid which precipi-

tated along with the picrate from the cooled solution were dissolved by adding cold absolute alcohol to the mixture. The picrate crystallizes in heavy black plates, which appear deep orange in color by transmitted light; m. p. 97–98.5°.

Anal. Calcd. for $C_{22}H_{20} \cdot C_6H_3O_7N_3$: N, 8.2. Found: N, 8.2.

9,10-Diethyl-1,2-benzanthracene-9,10-endo- α,β -succinic Anhydride.—A mixture of 0.5 g. of 9,10-diethyl-1,2-benzanthracene and 0.5 g. of maleic anhydride in 5 cc. of benzene was refluxed for twenty hours; on being cooled the solution deposited the addition compound in the form of stout, colorless needles; m. p. 215–217° with previous sintering; yield 0.5 g. No hydrocarbon was found unchanged.

Anal. Calcd. for $C_{26}H_{22}O_3$: C, 81.6; H, 5.8. Found: C, 81.1; H, 5.4.

When 0.1 g. of 9,10-diethyl-1,2-benzanthracene and 0.05 g. of maleic anhydride in 2 cc. of benzene was heated for twenty minutes only 20% of the addition product was formed. This was determined by converting the addition product to the water-soluble salt of the dicarboxylic acid by treatment with strong aqueous potassium hydroxide. When xylene was used and the mixture was heated for two hours an 84% yield of the adduct was formed. The addition product can be obtained rapidly by using a large excess of maleic anhydride. Thus, 0.5 g. of the hydrocarbon and 5 g. of maleic anhydride in 10 cc. of benzene was refluxed for two hours; the excess of anhydride was extracted from the cooled solution by means of water and the addition product obtained from the benzene was recrystallized from acetic anhydride.

5,9,10 -Trimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene (VI).—5-Methyl-1,2-benzanthraquinone was prepared by adding gradually 5.6 g. of powdered sodium dichromate dihydrate to a hot solution of 4.2 g. of 5-methyl-1,2-benzanthracene⁵ in 50 cc. of acetic acid. After the addition was complete, the solution was refluxed for ten minutes and then treated with dilute sulfuric acid to precipitate the 5-methyl-1,2-benzanthraquinone. After being filtered and dried, the latter was recrystallized from toluene, with addition of ethanol to the hot solution; yield, 4.06 g. (86%), which included 0.5 g. obtained from the mother liquor by evaporation and sublimation of the residue at 220° (0.3 mm.). The compound possessed the melting point reported by Cook, who prepared the compound by the same method.

To the cooled Grignard reagent prepared from 3.3 cc. of methyl iodide and 1.2 g. of magnesium in 20 cc. of ether was added 15 cc. of benzene, followed by 3.56 g. of 5-methyl-1,2-benzanthraquinone. After the mixture had been allowed to stand at room temperature for two hours, the clear tan-colored solution was hydrolyzed with ice-cold ammonium chloride solution. Most of the diol precipitated as fine colorless crystals at this point; from the ether-benzene solution more of the diol was obtained, making a total yield of 3.6 g. (91%). From dilute acetone the diol crystallized in small thin sheets; m. p. 204–206°. From the behavior of the compound it is not unlikely that both *cis* and *trans* forms were present. With concentrated sulfuric acid the diol gives a purplish-red color.

(5) Cook, *J. Chem. Soc.*, 1593 (1933); Bachmann and Wilds *This Journal*, 60, 624 (1938).

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.8; H, 6.6. Found: C, 82.8; H, 6.3.

To a suspension of 3 g. of the diol in 30 cc. of benzene was added a solution of 0.15 cc. of concentrated sulfuric acid in 60 cc. of methanol. As soon as all of the diol had gone into solution, the dimethyl ether of the diol began to crystallize as colorless needles. After purification in the manner described for the other diol ethers, the compound melted at 228–229°; yield 3 g. When a benzene suspension and solution of the total crude diol obtained from 3.56 g. of 5-methyl-1,2-benzanthraquinone was treated with methanol containing 0.2 cc. of sulfuric acid, 3.72 g. (85% on the basis of the quinone) of the diol dimethyl ether was obtained. The diol dimethyl ether gives a deep red color with concentrated sulfuric acid.

Anal. Calcd. for $C_{23}H_{24}O_2$: C, 83.1; H, 7.3. Found: C, 83.1; H, 7.3.

5,9,10-Trimethyl-1,2-benzanthracene (V).—A mixture of 2 g. of the aforementioned dimethyl ether and 0.28 g. of powdered sodium was allowed to react in 30 cc. of anhydrous ether in the usual manner; most of the diol dimethyl ether remained undissolved. After twenty-four hours the mixture was purple in color and contained a considerable amount of precipitate; the latter was still present after thirty-six hours and proved to be 5,9,10-trimethyl-1,2-benzanthracene (0.85 g., m. p. 127–128°). From the solution an additional 0.71 g. (m. p. 124–126°) of hydrocarbon was isolated, making a yield of 96%. After purification in the manner described for the other hydrocarbons, the 5,9,10-trimethyl-1,2-benzanthracene crystallized from acetone–alcohol in plates or leaflets which possessed a yellowish tinge; m. p. 127–128°. When

potassium was employed, the yield of crude, crystalline hydrocarbon was usually not greater than 80%.

Anal. Calcd. for $C_{21}H_{18}$: C, 93.3; H, 6.7. Found: C, 93.3; H, 6.2.

The picrate, prepared with excess of picric acid, crystallizes from absolute alcohol in beautiful black needles; m. p. 112–113°.

Anal. Calcd. for $C_{21}H_{18} \cdot C_6H_3O_7N_3$: N, 8.4. Found: N, 8.5.

5,9,10-Trimethyl-1,2-benzanthracene-9,10-endo- α,β -succinic Anhydride.—A solution of 0.5 g. of the hydrocarbon and 0.5 g. of maleic anhydride in 5 cc. of benzene was refluxed for one-half hour. The solution which was initially yellow became colorless and deposited crystals of the addition product. After cooling, 0.5 g. of the addition product was filtered off; it crystallizes from benzene in colorless needles; m. p. 250° with previous decomposition. The product obtained by evaporation of the benzene filtrate was completely soluble in hot aqueous potassium hydroxide, an indication that the addition of maleic anhydride to the hydrocarbon had been complete.

Anal. Calcd. for $C_{23}H_{20}O_4$: C, 81.5; H, 5.4. Found: C, 82.2; H, 5.1.

Summary

Three new polycyclic hydrocarbons, 9,10-dimethyl-1,2-benzanthracene, 9,10-diethyl-1,2-benzanthracene and 5,9,10-trimethyl-1,2-benzanthracene, have been synthesized for their possible cancer-producing properties.

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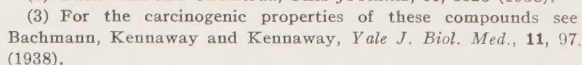
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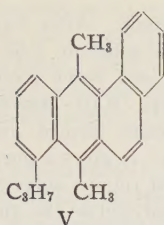
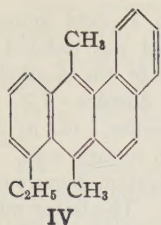
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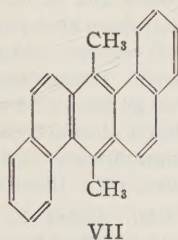
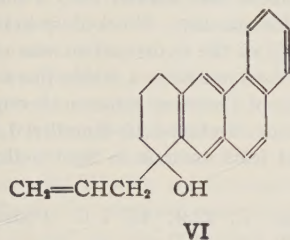
By W. E. BACHMANN AND J. M. CHEMERDA¹

(4) Bachmann and Bradbury, *J. Org. Chem.*, **2**, 175 (1937).





1,2-benzanthracene and ethylmagnesium bromide, followed by treatment of the resulting carbinol with palladium on charcoal as was done in the preparation of 5-methyl-1,2-benzanthracene.⁵ When the cyclic ketone was treated with *n*-propylmagnesium bromide, considerable reduction took place. The 5-*n*-propyl-1,2-benzanthracene was best prepared by the catalytic dehydration and isomerization of the carbinol VI, which was obtained in good yield by interaction of the cyclic ketone and allylmagnesium bromide.



Our reaction also offers a convenient preparation of 9,10-dimethyl-1,2,5,6-dibenzanthracene (VII). This hydrocarbon has been prepared previously by Cook⁶ by cautious reduction of the corresponding diol and by Akin and Bogert⁷ by means of the Pschorr synthesis.

Experimental

Reaction of Sodium with a Mixture of 9,10-Dimethyl-1,2-benzanthracene and Diol Dimethyl Ether.—A mixture of 1.0 g. of 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene and 0.80 g. of 9,10-dimethyl-1,2-benzanthracene (equimolar proportions) in 25 cc. of benzene and 25 cc. of ether was shaken with 0.14 g. of powdered sodium and some sharp glass particles. After one day's shaking, a nearly colorless solution was obtained and all of the sodium had reacted. From the solution 1.59 g. (99%) of the calculated amount of the 9,10-dimethyl-1,2-benzanthracene was isolated; m. p. 122–123°.

Reaction of 9,10-Dimethyl-9,10-disodio-9,10-dihydro-1,2-benzanthracene with Diol Dimethyl Ether.—The disodium derivative was prepared by shaking 1.25 g. of 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene with 0.36 g. of powdered sodium in 30 cc. of ether and 30 cc. of benzene. After a week, the solution had a color reminiscent of the permanganate ion. The

addition of 1.25 g. of the diol dimethyl ether did not decolorize the solution; the solution seemed to take on a brighter tinge of red. After a week, no further change was observed and the solution was treated with carbon dioxide to remove the disodium derivative. From the benzene-ether solution 0.75 g. (58%) of pure diol dimethyl ether was isolated. The mother liquor gave lower melting material from which no 9,10-dimethyl-1,2-benzanthracene could be isolated.

In another experiment, the disodium derivative was prepared by shaking the hydrocarbon with the theoretical amount of sodium. In the same manner as described above, 80% of the added diol dimethyl ether was recovered.

9,10 - Dimethyl - 9,10 - diethoxy - 9,10 - dihydro - 1,2-benzanthracene.—A suspension of 1.0 g. of 9,10-dimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene⁴ in 5 cc. of absolute alcohol was treated with 0.05 cc. of sulfuric acid in 1 cc. of absolute alcohol. In ten minutes a clear solution was obtained and the diol diethyl ether crystallized out. After standing at room temperature for one hour the diol diethyl ether was collected, dissolved in benzene and washed with ammonium hydroxide to remove traces of sulfuric acid. It is highly essential that the ether be as pure as possible for the successful preparation of the hydrocarbon in the sodium reaction. The benzene solution was concentrated, alcohol was added and the diol diethyl ether crystallized in clumps of colorless narrow prisms; yield 0.84 g., m. p. 167.5–171°. After two recrystallizations from benzene-alcohol the 9,10-dimethyl-9,10-diethoxy-9,10-dihydro-1,2-benzanthracene melted at 172–173.5°.

Anal. Calcd. for $C_{24}H_{26}O_2$: C, 83.2; H, 7.6. Found: C, 83.1; H, 7.4.

A mixture of 0.84 g. of the above diol diethyl ether and 0.11 g. of powdered sodium in 15 cc. of benzene and 20 cc. of ether was shaken with a half-dozen sharp glass particles. In the course of a day, a greenish-blue mixture was obtained. The mixture was decolorized with methanol and washed with dilute hydrochloric acid. By recrystallization of the product from acetone-alcohol, 0.38 g. (61%) of 9,10-dimethyl-1,2-benzanthracene was obtained.

9,10-Di-*n*-propyl-1,2-benzanthracene.—The reaction mixture from 5.16 g. of 1,2-benzanthraquinone and *n*-propylmagnesium bromide, obtained according to the procedure of Bachmann and Bradbury,⁴ was hydrolyzed and the solvent evaporated at room temperature. Treatment of the oil with a solution of 0.25 cc. of sulfuric acid in 50 cc. of methanol resulted in an immediate crystallization of the diol dimethyl ether. After standing overnight at room temperature, the diol dimethyl ether (3.9 g.) was filtered off and treated in the manner already described. From benzene-methanol, 3.25 g. of 9,10-di-*n*-propyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene was obtained as colorless needles; m. p. 174–176°. One recrystallization from benzene-ethyl acetate raised the melting point to 176.5–177.5°. The compound gives a brown color with sulfuric acid.

Anal. Calcd. for $C_{26}H_{30}O_2$: C, 83.4; H, 8.1. Found: C, 83.5; H, 8.2.

A mixture of 2.31 g. of the diol dimethyl ether in 25 cc.

(5) Bachmann and Wilds, *THIS JOURNAL*, **60**, 624 (1938).

(6) Cook, *J. Chem. Soc.*, 489 (1931).

(7) Akin and Bogert, *THIS JOURNAL*, **59**, 1564 (1937).

of benzene and 25 cc. of ether shaken with 0.28 g. of powdered sodium for one day gave 1.83 g. (95%) of **9,10-di-*n*-propyl-1,2-benzanthracene**; m. p. 98.5–100°. After purification through the picrate and recrystallization from benzene–alcohol, the hydrocarbon formed thick colorless needles; m. p. 100.5–101°.

Anal. Calcd. for $C_{24}H_{24}$: C, 92.3; H, 7.7. Found: C, 92.1; H, 7.5.

The **picrate** of the hydrocarbon crystallized from absolute alcohol in black needles; m. p. 107.5–108°.

Anal. Calcd. for $C_{24}H_{24} \cdot C_6H_3O_7N_3$: N, 8.1. Found: N, 8.0.

5-Ethyl-1,2-benzanthracene.—To a solution of the Grignard reagent prepared from 22 g. of ethyl bromide and 50 cc. of ether was added 50 cc. of benzene. To the ice-cold solution was added 13.8 g. of 5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene. After standing at room temperature for half an hour, the mixture was hydrolyzed with ice-cold ammonium chloride solution. The reaction product obtained by evaporation of the solvent was heated with 1.0 g. of palladium on charcoal⁸ at 310–320° for half an hour in an atmosphere of nitrogen. The cooled solid was extracted with acetone–benzene. After concentrating and adding alcohol, 9.95 g. of slightly yellow hydrocarbon was obtained; m. p. 115–117°. An additional 1.3 g. of hydrocarbon was obtained by treating the product in the mother liquor once more with the catalyst making a total yield of 79% based on the cyclic ketone. After distillation at 0.4 mm. the hydrocarbon crystallized from acetone–alcohol in colorless plates; yield, 9.3 g. (65%); m. p. 118–119°. Cook and his co-workers⁹ reported a melting point of 120° for the compound prepared from 5-ketodecahydro-1,2-benzanthracene.

In another run with 5.0 g. of the cyclic ketone, the product was heated with 10 g. of powdered potassium bisulfate at 150–160° for one hour. The benzene extract of the hydrocarbon was clarified and concentrated, by addition of alcohol giving 3.46 g. of **5-ethyl-7,8-dihydro-1,2-benzanthracene**. A sample of the hydrocarbon after sublimation under reduced pressure crystallized from alcohol in colorless prisms; m. p. 110–112°.

Anal. Calcd. for $C_{20}H_{18}$: C, 93.0; H, 7.0. Found: C, 92.9; H, 7.1.

Dehydrogenation of the dihydro derivative by palladium on charcoal⁸ at 330–340° for one hour gave the hydrocarbon in 70% yield.

5-Ethyl-9,10-dimethyl-1,2-benzanthracene.—Five grams of 5-ethyl-1,2-benzanthracene was dissolved in 50 cc. of hot acetic acid. After cooling to 70°, 5.81 g. of pure sodium dichromate dihydrate was added in portions and the mixture was heated on the steam-bath for an hour. The quinone was precipitated by the addition of 15% sulfuric acid. Recrystallization from acetone–alcohol gave 4.1 g. of 5-ethyl-1,2-benzanthraquinone; m. p. 96–98°. A second recrystallization gave 3.75 g.; m. p. 97–98° (Cook,⁹ 97–98°).

5-Ethyl-1,2-benzanthraquinone (3.75 g.) was added to an ice-cold solution of the Grignard reagent prepared from 4 cc. of methyl iodide and 12 cc. of ether and 12 cc.

of benzene. After hydrolysis with ice-cold ammonium chloride solution, 3.54 g. of the diol was isolated. Recrystallized twice from ethyl acetate the **5-ethyl-9,10-dimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene** formed microscopic needles; m. p. 201.5–204.5°. It gives a purple color with sulfuric acid. Since the diol retains solvent of crystallization tenaciously, it was analyzed as the dimethyl ether. The latter was prepared by treating a suspension of the diol (3.0 g.) in 15 cc. of methanol with a solution of 0.15 cc. of sulfuric acid in 5 cc. of methanol. After one hour at room temperature the diol dimethyl ether was filtered off and purified in the usual manner. Recrystallization from benzene–methanol gave colorless needles of **5-ethyl-9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene**; yield, 2.36 g.; m. p. 194–195°. Two more recrystallizations raised the melting point to 197–200°.

Anal. Calcd. for $C_{24}H_{26}O_2$: C, 83.2; H, 7.6. Found: C, 83.4; H, 7.9.

A mixture of 2.36 g. of the above diol dimethyl ether (m. p. 194–196°) and 0.31 g. of powdered sodium in 25 cc. of ether and 25 cc. of benzene was shaken with a half-dozen sharp glass particles for one day. Worked up in the usual manner, 1.56 g. (80%) of the hydrocarbon was obtained. The hydrocarbon does not form a stable picrate. After purification by passage of a benzene solution through a tower of anhydrous alumina, **5-ethyl-9,10-dimethyl-1,2-benzanthracene** crystallized from acetone in light yellow plates; m. p. 107–108°.

Anal. Calcd. for $C_{22}H_{20}$: C, 92.9; H, 7.1. Found: C, 92.6; H, 6.8.

5-*n*-Propyl-1,2-benzanthracene.—(a) A mixture of 10 g. of 5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene, 2 g. of magnesium, 20 cc. of ether and 40 cc. of benzene was placed in a dry flask equipped with a reflux condenser. When 10 cc. of allyl bromide was added, a vigorous reaction was initiated in a few minutes. The contents were swirled occasionally until all the cyclic ketone dissolved (ten to twenty minutes) the mixture being cooled in a pan of cold water when necessary. The product began to crystallize from the hot mixture. After twelve hours in a refrigerator, the product was filtered off, washed with benzene and hydrolyzed with ice-cold ammonium chloride solution. The carbinol which crystallized out was filtered off, dissolved in benzene to free it from magnesium salts and returned to the benzene solution of the carbinol. Spontaneous evaporation of the solution gave practically colorless carbinol; yield 9.87 g. (84%). From dilute methanol, **5-allyl-5-hydroxy-5,6,7,8-tetrahydro-1,2-benzanthracene** crystallizes in colorless needles; m. p. 82–82.5°. With sulfuric acid it gives a brown color.

Anal. Calcd. for $C_{21}H_{20}O$: C, 87.5; H, 7.0. Found: C, 87.3; H, 7.0.

Five grams of the allylcarbinol was heated with 0.5 g. of palladium on charcoal⁸ for half an hour at 300° in an atmosphere of nitrogen. At this temperature there was a sudden evolution of hydrogen which was reabsorbed for the most part by the end of the experiment. The cooled malodorous melt was extracted with acetone, filtered and allowed to evaporate spontaneously. A gum settled out on the bottom and crystalline material along the

(8) Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).

(9) Cook, Robinson and Gulden, *J. Chem. Soc.*, 393 (1937).

sides. These portions, distilled separately at 0.4 mm. and recrystallized from acetone-alcohol, gave pure colorless needles of 5-*n*-propyl-1,2-benzanthracene; yield 3.55 g.; m. p. 90–92°. Cook and Haslewood¹⁰ prepared the compound (m. p. 92°) from 5-keto-dodecahydro-1,2-benzanthracene.

(b) Five grams of 5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene was added to an ice-cold solution of the Grignard reagent prepared from 4 cc. of *n*-propylmagnesium bromide and 20 cc. of ether followed by the addition of 20 cc. of benzene. The mixture was kept in a refrigerator for twenty-four hours and the crystalline product was filtered off and washed with benzene. The crystalline material was hydrolyzed with ice-cold ammonium chloride solution containing a little benzene. By spontaneous evaporation of the benzene solution and trituration of the residue with benzene-ligroin, 2.2 g. of 5-*n*-propyl-5-hydroxy-5,6,7,8-tetrahydro-1,2-benzanthracene was obtained. The carbinol crystallized from benzene-ligroin in colorless threads; m. p. 107–108.5°. With sulfuric acid it gives a brownish-yellow color. It was not obtained analytically pure. By dehydrating the carbinol by heating with formic acid and dehydrogenating the product with palladium on charcoal, a 69% yield of 5-*n*-propyl-1,2-benzanthracene (m. p. 86–88°) was obtained.

5-*n*-Propyl-9,10-dimethyl-1,2-benzanthracene.—In the same manner as described for the ethyl homolog, 4.42 g. of 5-*n*-propyl-1,2-benzanthraquinone (obtained in 66% yield by the oxidation of 5-*n*-propyl-1,2-benzanthracene) was treated with methylmagnesium iodide. The clear yellow gum obtained was scratched until crystallization set in and the diol triturated with benzene-ligroin; yield 3.9 g.; m. p. 160–161°. 5-*n*-Propyl-9,10-dimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene crystallized from ligroin-ethyl acetate in microscopic needles; m. p. 161.5–163°. With sulfuric acid it gives a purple color. It retains solvent of crystallization tenaciously and was analyzed as the dimethyl ether. In the manner previously described, 3.0 g. of the diol dimethyl ether was obtained from 3.4 g. of the diol. 5-*n*-Propyl-9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene crystallizes from benzene-methanol in colorless rectangular prisms; m. p. 157–159°.

Anal. Calcd. for $C_{25}H_{28}O_2$: C, 83.3; H, 7.8. Found: C, 83.3; H, 7.9.

A mixture of 2.23 g. of the diol dimethyl ether reacted with 0.29 g. of powdered sodium in 25 cc. of ether and 25 cc. of benzene in the manner previously described to give 1.64 g. (89%) of 5-*n*-propyl-9,10-dimethyl-1,2-benzanthracene. Purified by passage of a benzene solution of the hydrocarbon through anhydrous alumina and crystallized from acetone-alcohol, the hydrocarbon formed yellowish nacreous plates; m. p. 84–85°.

Anal. Calcd. for $C_{23}H_{22}$: C, 92.6; H, 7.4. Found: C, 92.4; H, 7.7.

9,10-Dimethyl-1,2,5,6-dibenzanthracene.—One and one-half grams of the crude methyl diol, obtained according to Cook's⁶ procedure, was treated with a solution of 0.2 cc. of sulfuric acid in 10 cc. of methanol and 20 cc. of benzene. The diol dissolved and the diol dimethyl ether crystallized in fine needles. After purification in the usual manner the 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2,5,6-dibenzanthracene (1.2 g.) crystallized from benzene in fine narrow colorless prisms; m. p. 310–320° with decomposition.

Anal. Calcd. for $C_{26}H_{24}O_2$: C, 84.8; H, 6.6. Found: C, 84.7; H, 6.7.

A mixture of 0.092 g. of powdered sodium and 0.74 g. of the diol dimethyl ether in 20 cc. of ether and 20 cc. of benzene was shaken for two days. A yield of 0.52 g. (85%) of hydrocarbon was obtained; m. p. 202–205°. From the mother liquor an additional 0.06 g. was obtained which gave 0.07 g. of fairly pure picrate; m. p. 174–176°.

The first crop was picrated in benzene and the benzene solution of the regenerated hydrocarbon passed through anhydrous alumina. From benzene the 9,10-dimethyl-1,2,5,6-dibenzanthracene crystallized in glistening yellow plates; m. p. 205.5–206.5°, the same melting point reported by Cook.⁶

9,10-Dimethyl-1,2,5,6-dibenzanthracene and picric acid dissolved in hot alcohol containing a little benzene deposited bright red needles of a *dipicrate*; m. p. 175°.

Anal. Calcd. for $C_{24}H_{18} \cdot 2C_6H_3O_7N_3$: N, 11.0. Found: N, 11.0.

Care must be exercised to avoid undue exposure of solutions of the hydrocarbon to light, for the hydrocarbon readily forms a peroxide. In one experiment, after purification, colorless needles of the peroxide were obtained instead of the usual yellow plates; m. p. 206–207° with decomposition. When placed in a bath at 200°, a melting point of 218–219° with bubbling and complete decomposition was observed. This same compound was prepared by exposure to sunlight of a solution of 0.10 g. of the hydrocarbon in 5 cc. of benzene. After forty-five minutes, 0.07 g. of clumps of colorless needles of 9,10-dimethyl-1,2,5,6-dibenzanthracene peroxide was filtered off; m. p. 212–213° with decomposition when placed in the bath at 200°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.2; H, 5.4. Found: C, 84.4; H, 5.5.

Summary

The mechanism by which 9,10-dimethyl-1,2-benzanthracene is formed by interaction of sodium and 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene has been investigated.

5-Ethyl- and 5-*n*-propyl-9,10-dimethyl-1,2-benzanthracene, 9,10-di-*n*-propyl-1,2-benzanthracene and 9,10-dimethyl-1,2,5,6-dibenzanthracene have been prepared.

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(10) Cook and Haslewood, *J. Chem. Soc.*, 428 (1934).

